CLAIMS

We claim:

1. A humanized CC49 antibody, comprising a non-conservative amino acid substitution in a light chain complementarity determining region 3 of the CC49 antibody, or functional fragment of the humanized CC49 antibody, that has a high binding affinity for TAG-72.

2. The antibody of claim 1, wherein the non-conservative substitution is a tyrosine to proline substitution.

3. The antibody of claim 1, wherein the non-conservative substitution is at position 91.

4. The antibody of claim 1, wherein the non-conservative substitution is at a residue that is a ligand contact residue.

5. The antibody of claim 1, wherein the functional fragment is an Fab fragment, an Fv fragment, or an $F(ab')_2$ fragment.

6. The antibody of claim 1, wherein a light chain complementarity determining region 1 and a light chain complementarity determining region 2 are from a human antibody.

7. The antibody of claim 1, wherein the light chain complementarity determining region 3, a heavy chain complementarity determining region 1, a heavy chain

complementarity determining region 2, and a heavy chain complementarity determining region 3 are from a murine CC49 antibody.

8. The antibody of claim 1, wherein the high binding affinity is at least about 1.2 x 10^{-8} M.

9. The antibody of claim 8, wherein the high binding affinity is at least about 1.5 x 10^{-8}, about 2.0 x 10^{-8}, about 2.5 x 10^{-8}, about 3.0 x 10^{-8}, about 3.5 x 10^{-8}, about 4.0 x 10^{-8}, about 4.5 x 10^{-8}, or about 5.0 x 10^{-8} M.

10. The antibody of claim 1, wherein the antibody is minimally immunogenic.

11. The antibody of claim 1, wherein the antibody further comprises an effector molecule.

12. The antibody of claim 11, wherein the effector molecule is a detectable label.

13. The antibody of claim 12, wherein the detectable label comprises a radioactive isotope, an enzyme substrate, a co-factor, a ligand, a chemiluminescent agent, a fluorescent agent, a hapten, or an enzyme.

14. The antibody of claim 11, wherein the effector molecule is a toxin.

15. The antibody of claim 14, wherein the toxin is a chemotherapeutic drug, a radioactive isotope, a bacterial toxin, a viral toxin, a cytokine or a venom protein.

16. The antibody of claim 1, further comprising at least one additional non-conservative amino acid substitution in a light chain complementarity determining region.

17. The antibody of claim 16, wherein the light chain complementarity determining region is a light chain complementarity determining region 1, a light chain complementarity determining region 2, or a light chain complementarity determining region 3.

18. The antibody of claim 1, further comprising at least one non-conservative amino acid substitution in a heavy chain complementarity determining region.

19. The antibody of claim 18, wherein the heavy chain complementarity determining region is a heavy chain complementarity determining region 1, a heavy chain complementarity determining region 2, or a heavy chain complementarity determining region 3.

20. A humanized CC49 antibody, wherein a nucleic acid sequence encoding the antibody has an ATCC Accession number comprising ATCC Accession number PTA-4182 or ATCC Accession number PTA-4183.

21. A nucleic acid molecule encoding the humanized monoclonal antibody of claim 1.

22. A vector comprising the nucleic acid of claim 21.

23. A humanized CC49 antibody, comprising:

a variable light framework region and a variable heavy framework region of a human antibody;

a complementarity determining region, wherein at least one complementarity determining region is from the human antibody and the remaining complementarity determining regions are from a murine CC49 antibody;

a non-conservative substitution of a first residue in a light chain complementarity determining region 3; and

a substitution of a second residue in a complementarity determining region of the human CC49 antibody;

wherein the humanized CC49 antibody has a high binding affinity for TAG-72 and is minimally immunogenic.

24. The antibody of claim 23, wherein the non-conservative substitution is a tyrosine to proline substitution.

25. The antibody of claim 23, wherein the non-conservative substitution is at position 91.

26. The antibody of claim 25, wherein the non-conservative substitution at position 91 is a tyrosine to proline substitution.

27. The antibody of claim 23, wherein the antibody further comprises an effector molecule.

28. The antibody of claim 27, wherein the effector molecule is a detectable label.

29. The antibody of claim 28, wherein the detectable label comprises a radioactive isotope, an enzyme substrate, a co-factor, a ligand, a chemiluminescent agent, a fluorescent agent, a hapten, or an enzyme.

30. The antibody of claim 27, wherein the effector molecule is a toxin.

31. The antibody of claim 30, wherein the toxin is a chemotherapeutic drug, a radioactive isotope, a bacterial toxin, a viral toxin, a cytokine or a venom protein.

32. A method of detecting a TAG-72-expressing tumor in a subject, comprising:

contacting a sample obtained from the subject with the antibody of claim 1 for a sufficient amount of time to form an immune complex;

detecting the presence of the immune complex, wherein the presence of the immune complex demonstrates the presence of the TAG-72-expressing tumor.

33. The method of claim 32, wherein the tumor is a colorectal tumor, a gastric tumor, a pancreatic tumor, a breast tumor, a lung tumor, an adenocarcinoma, or an ovarian tumor.

34. The method of claim 32, wherein the antibody further comprises an effector molecule.

35. The method of claim 34, wherein the effector molecule is a detectable label.

36. The method of claim 35, wherein the detectable label comprises a radioactive isotope, an enzyme substrate, a co-factor, a ligand, a chemiluminescent agent, a fluorescent agent, a hapten, or an enzyme.

37. The method of claim 32, further comprising contacting the antibody with a secondary antibody.

38. The method of claim 37, wherein the secondary antibody further comprises a detectable label.

39. A method of detecting a TAG-72-expressing tumor in a subject, comprising:

administering the antibody of claim 1 to the subject for a sufficient amount of time to form an immune complex;

detecting the presence of the immune complex, wherein the presence of the immune complex demonstrates the presence of the TAG-72-expressing tumor.

40. The method of claim 39, wherein the antibody further comprises an effector molecule.

41. The method of claim 40, wherein the effector molecule is a detectable label.

42. The method of claim 41, wherein the detectable label comprises a radioactive isotope, an enzyme substrate, a co-factor, a ligand, a chemiluminescent agent, a fluorescent agent, a hapten, or an enzyme.

43. The method of claim 39, wherein the tumor is a colorectal tumor, a gastric tumor, a pancreatic tumor, a breast tumor, a lung tumor, an adenocarcinoma, or an ovarian tumor.

44. A method of treating a subject having a tumor that expresses TAG-72, comprising administering to the subject a therapeutically effective amount of the antibody of claim 1, wherein administering the therapeutically effective amount of the antibody of claim 1 inhibits the growth of the tumor or reduces the size of the tumor, thereby treating the subject.

45. The method of claim 44, wherein the administration of a therapeutically effective amount of the antibody of claim 1 does not elicit a human anti-murine antibody response in a subject.

46. The method of claim 44, wherein the tumor is a colorectal tumor, a gastric tumor, a pancreatic tumor, a breast tumor, a lung tumor, an adenocarcinoma, or an ovarian tumor.

47. The method of claim 44, wherein the antibody further comprises an effector molecule.

48. The method of claim 47, wherein the effector molecule is a toxin.

49. The method of claim 48, wherein the toxin is a chemotherapeutic drug, a radioactive isotope, a bacterial toxin, a viral toxin, a cytokine, or a venom protein.

50. The method of claim 49, wherein the antibody comprising a radioactive isotope is used in radioimmunotherapy.

51. A method of treating a subject having a tumor that expresses TAG-72, comprising:

administering the antibody of claim 1 to the subject for a sufficient amount of time to form an immune complex, wherein the antibody comprises a radioactive isotope;

detecting the presence of the immune complex with a hand-held gamma counter, wherein the presence of the immune complex demonstrates the presence of the TAG-72-expressing tumor; and

removing the tumor surgically, thereby treating the subject.

52. A pharmaceutical composition comprising a therapeutically effective amount of the antibody of claim 1 in a pharmaceutically acceptable carrier.

53. A kit, comprising a container comprising the antibody of claim 1.

54. The kit of claim 53, further comprising a container containing an antigen, a container containing a secondary antibody conjugated to a chemical compound, instructions for using the kit, or any combination thereof.